Laryngeal carcinoma: five-year survival and patterns of failure in 202 consecutive patients treated with primary or post-operative radiotherapy in Hong Kong

Alexander C Vlantis, FCS(SA)ORL, Brian K H YU, FRCR*, Raymond K Y Tsang, FRCSEd(ORL), Michael K M Kam, FRCR*, Phoebe S Y Lo, MSc, C Andrew van Hasselt, MMed(OTOL)

Abstract

Objectives: We aimed to conduct a retrospective analysis of patients treated with radiotherapy for laryngeal carcinoma at a single institution.

Methods: We analysed data from 202 consecutive patients treated with primary or post-operative radiotherapy for laryngeal carcinoma over a 10-year period.

Results: Sixty-nine patients had a T_1 , 65 a T_2 , 39 a T_3 and 29 a T_4 lesion. Forty-one patients were nodepositive. The clinical stage was I in 67 patients, II in 53, III in 36 and IV in 46. Primary radiotherapy was given to 152 patients. The median follow up was 60 months. The five-year overall local control rate was 86 per cent, the ultimate local control rate was 93 per cent, the five-year regional control rate was 96 per cent, the five-year relapse-free survival rate was 82 per cent and the five-year overall survival rate was 69 per cent.

Conclusions: Patients with laryngeal carcinoma treated with primary or post-operative radiotherapy had a five-year overall survival rate of 69 per cent.

Key words: Larynx; Carcinoma; Radiotherapy; Survival

Introduction

Radiotherapy was used primarily or post-operatively to treat all patients with laryngeal carcinoma at the Prince of Wales Hospital in Hong Kong between 1990 and 1999. Surgery was performed for advanced cases prior to radiotherapy or as a salvage procedure. This study is a retrospective analysis of the five-year survival rates and patterns of failure of all patients with laryngeal carcinoma treated with either radiotherapy, or surgery and post-operative radiotherapy, with the intention to cure, during the 10-year study period. Published results from other institutions are used for perspective. Chemoradiotherapy was introduced during the study period in a trial setting for advanced laryngeal carcinomas, prompted by reports that it could lead to organ preservation without compromising overall survival and that locoregional control and survival may be improved.¹ Endolaryngeal laser surgery was not used to treat laryngeal carcinoma during the study period.

Materials and methods

We reviewed the medical records of 271 consecutive patients who received radiotherapy for laryngeal

carcinoma at the Prince of Wales Hospital, Hong Kong, between January 1990 and December 1999. Data from patients treated with a standardized protocol, with the intent to cure, were analysed. Sixty-nine patients were excluded from the analysis for the following reasons: two patients had carcinoma in situ, five patients were given concurrent chemotherapy, 22 patients received palliative radiotherapy and 40 patients received radiotherapy with fraction sizes > 2.5 Gray (Gy). Two hundred and two patients were eligible for analysis. All tumours were staged according to the fifth edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual.² All patients received either primary radiotherapy or underwent surgery and received postoperative radiotherapy.

For primary radiotherapy, the clinical target volume included the primary tumour with 1.5 cm margins. Bilateral cervical nodal sites were irradiated if the primary tumour was a T_3-T_4 glottic carcinoma, a supraglottic or subglottic carcinoma of any T stage or if there were cervical nodal metastases.

Patients requiring a pretreatment tracheostomy or patients with a bulky T_3 or T_4 lesion of the larynx were offered a total laryngectomy followed by

From the Departments of Surgery and *Clinical Oncology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR, China. Accepted for publication: 18 August 2005. post-operative radiotherapy as treatment for the primary. A bulky T_3 lesion was taken as one that was potentially able to compromise the patient's airway. Post-operative radiotherapy was given to the surgical bed for T_3-T_4 primary tumours, N_2-N_3 disease, extracapsular extension of nodal disease and close resection margins (<1 cm), and to cervical nodal sites at risk of containing subclinical disease. Primary radiotherapy was given if a patient refused surgery. Patients were followed up at regular intervals for a period of five years after treatment.

Statistical analysis

The computer programme SPSS[®] 13.0 for Windows was used to analyse the data. The date of treatment was taken as the last day of radiotherapy for those patients who received primary radiotherapy and as the day of surgery for those patients who underwent primary surgery and who were given post-operative radiotherapy. The Chi-squared test or Fisher's exact test were used to examine the demographic background of the subjects between treatment modalities. Overall survival was measured from the date of treatment to the date of the last follow up, at or within five years of treatment, or to the date of death from any cause. Initial local control was measured from the date of treatment to the date of first local recurrence. Ultimate local control was measured from the date of treatment to the date of the second or subsequent local failure following treatment of the first local recurrence. Patients who were lost to follow up were censored on the date of their last follow up and their disease status was based on that documented at their last follow up. Persistent disease was defined as the presence of disease within six months of the date of treatment and included local and/or regional and/or distant disease. For patients who had persistent disease following radiotherapy, the time to relapse was taken as zero. The univariate Kaplan-Meier method was used to estimate the probability of local relapse, initial and ultimate local control, relapse-free survival and overall survival. Differences between selected factors, such as gender, age groups, tumour (T) stages, nodal (N) stages, group stage, treatment modalities (surgery and post-operative radiotherapy, or primary radiotherapy) and radiotherapy fraction size, were assessed using the log-rank test. Factors with $p \le 0.5$ from the preliminary analysis were eligible for the multivariate Cox regression analysis. The level of significant was set at p < 0.05.

Results and analysis

Patient demographic characteristics

The median age of the study patients (n = 202) was 68 years (range 36–85 years). Table I describes the patients' characteristics. Patients receiving primary radiotherapy and those who underwent primary surgery with post-operative radiotherapy were similar in age (p = 0.253) and gender (p = 1.000). Patients in the primary surgery with post-operative radiotherapy group were more likely to have advanced-stage disease (stages I + II versus stages III + IV, p < 0.001). More than half of the patients in the primary surgery with post-operative radiotherapy group suffered from supraglottic carcinoma, while the majority of subjects (68 per cent) in the primary radiotherapy group had glottic carcinoma.

Radiotherapy complications

Radiotherapy was well tolerated. Patients experienced mild to moderate acute radiation laryngitis with some degree of hoarseness. Most patients also had mild to moderate acute radiation pharyngitis and skin reactions. These acute reactions subsided two to three weeks after completing radiotherapy. There were no cases of acute perichondritis or chondritis nor were there any cases of late radiationinduced laryngeal chondronecrosis. No patient required surgical treatment for late radiotherapy complications. At the last follow up, all recurrencefree patients who had a remaining larynx had a voice which ranged from normal to mildly or moderately hoarse. Endoscopically, mild to moderate laryngeal oedema and telangiectasia were common manifestations of late radiotherapy changes.

Follow-up status

Table II summarizes the follow-up status of the patients. Of the 202 study patients, 61 (30 per cent) died during follow up, 118 (58 per cent) were alive at the time of this study (105 alive with no evidence of disease) and 23 (11 per cent) were lost to follow up. The median follow-up period of patients who were alive at the time of the study was 60 months (range 31–60 months). Eighteen patients (9 per cent) had persistent disease following primary radiotherapy. Three of these patients were salvaged with a total laryngectomy; two of them were alive without any evidence of disease at 60 months and one was lost to follow up. Three patients with either persistent local, regional or locoregional disease were lost to follow up. Twelve patients of this group died, four with local disease, three with regional disease and five with distant metastases.

Local failure and salvage treatment

There was local relapse at the primary site in 24 patients (17 per cent). Five of these patients had a simultaneous regional recurrence. The median interval between the date of treatment and the detection of recurrence was 16 months (range 7–56 months). Seventy-five per cent of the local recurrences occurred within the first two years. Of the 24 patients, two were re-irradiated, 11 were treated with salvage surgery and 11 received no further treatment (they either refused further treatment).

Of the two patients who were re-irradiated, one died eight months after re-irradiation and the other underwent a salvage laryngectomy for a second local relapse at 19 months after the re-irradiation. At the time of the study, this patient was alive and

Demographical and clinical characteristics		Total $(n = 202)$				
	Primary RT $(n = 152)$		Primary surgery + post-op RT ($n = 50$)			
	n	%	п	%	п	%
$ \frac{Age (years)}{\leq 60} $	33	21.7	15	30.0	48	23.8
200 Condon	119	/0.5	55	70.0	154	70.2
Female Male	14 138	9.2 90.8	4 46	8.0 92.0	18 184	8.9 91.1
Disease stage at primary site						
T ₁ T ₂ T ₃ T.	68 58 22 4	44.7 38.2 14.5 2.6	1 7 17 25	2.0 14.0 34.0 50.0	69 65 39 29	34.1 32.2 19.3 14 4
Nodal stage	·	2.0	20	20.0	27	1
N_0 N ₁ or N ₂ or N ₃	137 15	90.1 9.9	24 26	48.0 52.0	161 41	79.7 20.3
AJCC disease stage						
I II III IV	67 52 23 10	44.1 34.2 15.1 6.6	0 1 13 36	0 2.0 26.0 72.0	67 53 36 46	33.2 26.2 17.8 22.8
Tumour site						
Supraglottis Subglottis Glottis Transglottis Missing data	44 1 104 2 1	28.9 0.7 68.4 1.3 0.7	26 0 15 9 0	52.0 0 30.0 18.0 0	70 1 119 11 1	34.7 0.5 58.9 5.4 0.5
Tracheostomy before RT No Yes Missing data	123 9 20	80.9 5.9 13.2	6 38 6	12.0 76.0 12.0	129 47 26	63.8 23.3 12.9

TABLE I PATIENT CHARACTERISTICS

RT = radiotherapy; post-op = post-operative; AJCC = American Joint Committee on Cancer

had been without disease for more than 60 months after his laryngectomy.

In total, 12 patients underwent salvage surgery for a local relapse; 10 patients underwent a total laryngectomy and two patients underwent a total laryngectomy with a radical neck dissection. At the time of the study, one of the 12 patients was alive with distant metastases, 10 patients were alive without any evidence of disease, with a median survival of 60 months (range 35–60 months or more), and one patient died of a second primary malignancy 25 months after the salvage surgery.

Of the 11 patients who did not receive salvage treatment, five died of local disease, four died of locoregional disease, one died of local and distant disease, and one was lost to follow up three months after the diagnosis of local recurrence. The median interval between the diagnosis of the local recurrence

PATIENT FOLLOW UP*							
Patient status	Alive	Dead					
	Compliant with FU	Lost to FU					
No evidence of any recurrence throughout the study period	105	15	19 (Died of other cause) 8 (Died of other malignancy) 6 (Unknown status)				
Persistent disease following RT	2	4	12				
Relapse with local disease [†]	10	0	9				
Relapse with regional disease [†]	0	2	3				
Relapse with locoregional disease [†]	1	1	3				
Presents with distant metastasis	0	1	1				
Total	118	23	61				

TABLE II

*Based on a five-year assessment, n = 202

 \dagger First relapse. FU = follow up; RT = radiotherapy

and death was 7.5 months (range 0-23 months) and the median overall survival for these 11 patients from the date of treatment was 21.5 months (range 10-50 months).

The initial T stages of the 24 patients with local relapse were as follows: T_1 (n = 7), T_2 (n = 9), T_3 (n = 4) and T_4 (n = 4). Multivariate analysis revealed that the type of primary treatment received, radiotherapy versus surgery, was significantly associated with local failure (p = 0.005). This was probably due to the fact that local failure did not usually occur in patients who had undergone laryngectomy. In contrast, T stage (p = 0.788), N stage (p = 0.420), group stage (p = 0.361) and gender (p = 0.729) did not significantly affect this endpoint.

The five-year overall local control rate for the entire group (n = 202) was 86 per cent. The fiveyear local control rates for stages T₁, T₂, T₃, and T₄ were 88 per cent, 83 per cent, 83 per cent and 80 per cent, respectively. The ultimate local control rate for the entire group of patients (n = 202) was 93 per cent. The ultimate local control rates for stages T₁, T₂, T₃, and T₄ were 98 per cent, 92 per cent, 85 per cent and 79 per cent, respectively.

Regional recurrence and salvage treatment

Ten patients (5 per cent) developed regional recurrence (five regional and five locoregional). Two of the five patients who had regional relapse had a simultaneous distant metastasis; none of these five patients received treatment for their recurrence. Three died and two were lost to follow up. Of the five patients who developed locoregional recurrence, one remained disease-free and survived for more than 60 months after a salvage laryngectomy and radical neck dissection done 19 months after primary radiotherapy, three died, and one was lost to follow up. The T stages of the 10 patients with regional relapse were as follows: T_2 (n = 4), T_3 (n = 5) and T_4 (n = 1). The N stages were: N_0 (n = 6), N₂ (n = 3) and N₃ (n = 1). Multivariate analysis showed that none of the analysed factors significantly influenced regional failure (all p values >0.05). For the entire group of patients (n = 202), the probability of a five-year regional control was 96 per cent. The median time to regional recurrence was 15.5 months (range 9–40 months).

Relapse-free survival

The five-year relapse-free survival rate for the entire group, derived from the Kaplan–Meier survival curve, was 82 per cent. The rates for T₁, T₂, T₃, and T₄ were 88 per cent, 81 per cent, 70 per cent and 68 per cent, respectively (Figure 1). There was a significant difference in the survival rate between the N₀ group (84 per cent) and the N₁/N₂/N₃ group (63 per cent) (p = 0.025) (Figure 2). The relapse-free survival rates by AJCC group stages I, II, III, and IV were 89 per cent, 82 per cent, 77 per cent and 65 per cent, respectively. There were significant differences between AJCC group stages (stages I + II versus stages III + IV, p = 0.0157), T stages



Fig. 1

Relapse-free patient survival rates (product-limit method) at 5 years: T₁, 88%; T₂, 81%; T₃, 70%; T₄, 68%.



Relapse-free patient survival rates (product-limit method) at 5 years, stratified for N_0 and N_+ nodal status.

 $(T_1 + T_2 \text{ versus } T_3 + T_4, p = 0.0313)$ and N stages (N₀ versus N₁ + N₂ + N₃, p = 0.025) in the univariate analysis. None of the analysed factors were significant in the multivariate analysis.

Overall survival

The probability of a five-year overall survival for the entire group of patients (n = 202) was 69 per cent. The Kaplan-Meier survival curves stratified by T stage, N stage and AJCC group stage are presented in Figures 3, 4 and 5, respectively. There was no significant difference in overall survival between women and men (p = 0.177), between radiotherapy fraction sizes (p = 0.3616) and between treatment modalities (p = 0.1033) in the univariate analysis. Results of multivariate analysis showed that age (p = 0.001)and T stage (p = 0.002) were the significant factors that affected overall survival (Table III). Three of the 48 patients (6 per cent) who were 60 years old or younger died, two due to persistent disease with distant metastases and one whose status was unknown. For patients older than 60 years, 58 of the 154 patients (38 per cent) died. Of these, 26 patients (45 per cent) died with disease, while the status of the others who died was unknown.



Fig. 3

Overall patient survival (Kaplan–Meier curves) according to tumour (T) stage. Significance detected in the following comparisons: $T_1 vs T_3 (p = 0.0006)$; $T_1 vs T_4 (p = 0.0001)$; $T_2 vs T_4 (p = 0.0304)$.



Overall patient survival (Kaplan–Meier curves) according to nodal (N) stage.



Fig. 5

Overall survival (Kaplan-Meier curves) according to group American Joint Committee on Cancer stage. Significance detected in the following comparisons: stage I vs stage III (p = 0.0213); stage I vs stage IV (p < 0.0001); stage II vs stage IV (p = 0.0015).

TABLE III OVERALL PATIENT SURVIVAL OUTCOME⁴

Prognostic factor	RR	95% CI	р	
Age (years)				
≤ 60	1			
>60	7.85	2.45-25.12	0.001†	
Gender				
Female	1			
Male	2.61	0.79-8.68	0.117	
Tumour stage				
T_1 (reference)	1			
T_2	1.86	0.89-3.89	0.098	
T_3	3.92	1.72-8.98	0.001†	
Γ_4	6.56	2.41-17.83	< 0.001†	
Nodal stage				
N ₀	1	0.06 0.01	0.070	
N_1 or N_2 or N_3	1.75	0.96-3.21	0.070	
Treatment modality				
Primary surgery +	1			
post-op RT				
Primary RT	1.96	0.93 - 4.12	0.075	
RT fraction size				
2 Gy/Fr	1			
2.5 Gy/Fr	0.84	0.46 - 1.55	0.581	

*Cox regression analysis

 $\dagger p < 0.005$. RR = relative risk; CI = confidence interval; post-op = post-operative; RT = radiotherapy

Discussion

The present material represents a series of consecutive patients with laryngeal carcinoma who were treated, with the intention to cure, with either radiotherapy, or surgery and post-operative radiotherapy, at the Prince of Wales Hospital, Hong Kong, between 1990 and 1999. Patients were treated primarily with external beam radiotherapy or underwent a total laryngectomy and received postoperative radiotherapy. Patients offered a total laryngectomy were those with bulky (unfavourable) T₃ lesions, T₄ lesions and those with airway obstruction requiring a pretreatment tracheostomy.

The goal of treating early glottic carcinoma is tumour control and voice preservation without serious side effects.³ Current options include cordstripping, endoscopic laser excision, partial laryngeal surgery and radiotherapy. Patients in this series with T_1 glottic carcinomas were treated with radiotherapy. The literature tends to support the use of primary radiotherapy for early glottic lesions, especially for large T_1 lesions for which surgery would require relatively significant soft tissue resection with compromise of voice quality.³⁻⁶ Although laser surgery has recently gained some popularity as an alternative to radiotherapy for treating small glottic lesions,^{4,7,8} there is some loss in the quality of voice when compared with treatment with radiotherapy.^{4,9} The cure and larynx preservation rates are however similar between the two modalities of radiotherapy and laser,^{4,10,11} and so there remains no clear treatment modality of choice.¹²

Patients with T_2 glottic lesions in this series were treated with primary radiotherapy. Other treatment options include partial laryngeal surgery, which Chevalier *et al.* found gave a 95 per cent locoregional

control and organ preservation rate,¹³ but usually achieved at the expense of voice quality.⁴ Laser resection of T_2 glottic tumours is possible, although series in the literature remain limited.⁷

Patients with T_3 glottic lesions in whom the airway was not compromised, as well as patients with bulky T_3 disease who refused a total laryngectomy, were treated with primary radiotherapy. Patients with T_4 lesions, as well as patients who required a pretreatment tracheostomy, were treated with primary surgery and post-operative radiotherapy. Patients who refused a total laryngectomy were treated with radiotherapy.

The treatment of T_1-T_2 supraglottic carcinomas with surgery, laser resection or radiotherapy gives similar results, according to the literature, with a five-year disease-specific survival rate of 72–79 per cent, which includes salvage surgery.¹⁴ The initial local control rates for T₁ supraglottic lesions range from 70 to 100 per cent and for T_2 lesions from 61 to 87 per cent.^{3,15–20} The local control rates after radiotherapy for T_3 supraglottic lesions range from approximately 54 per cent to 70 per cent.^{15,16–21} The local control rates after radiotherapy for T_4 supraglottic lesions range from approximately 29 per cent to 65 per cent.^{15–21} In one series, 21 per cent of patients developed local recurrence after radiotherapy for supraglottic lesions, of which just under half (45 per cent) were successfully salvaged.²⁰ In the same series, the five-year absolute survival rates for supraglottic lesions were 65 per cent for stage I, 59 per cent for stage II, 53 per cent for stage III and 33 per cent for stage IVA.

In Harwood's series, all six patients with T_1 or T_2 subglottic lesions who were treated with radiotherapy were controlled locally after one to six years of follow up.¹⁵ However, in the same series, seven of 14 patients with T_3 or T_4 subglottic lesions died of their disease.¹⁵ Paisley *et al.* reported that, for their patients with subglottic lesions who were treated with either primary radiotherapy or surgery and post-operative radiotherapy, the local control rates for T_1 and T_2 lesions were 65 per cent, for T_3 lesions were 50 per cent and for T_4 lesions were 42 per cent.²²

The local recurrence rate in our series for T_1 lesions of all laryngeal sites treated with primary radiotherapy was 10 per cent (seven patients), which is in keeping with that reported by Jørgensen *et al.*, whose series had a five-year recurrence rate of 12 per cent after primary radiotherapy,⁴ and Eckel, whose series showed a recurrence rate of 13 per cent after laser resection.²³ In the literature, the initial local control with radiotherapy for T_1 glottic lesions ranges from 81 to 93 per cent and the ultimate local control ranges from 91 to 99 per cent.^{3,15} Therefore, other factors, such as quality of life, voice quality, local resources and local expertise become important when choosing the treatment modality.²⁴

Nine patients (16 per cent) with T_2 laryngeal lesions developed local recurrence after radiotherapy in our series. Jørgensen *et al.* reported a locoregional control of 67 per cent in patients with T_2 lesions treated with radiotherapy, although they did not

report the specific local failure rate.⁴ In the literature, the initial local control with radiotherapy for T_2 glottic lesions ranges from 67 to 88 per cent and the ultimate local control ranges from 79 to 95 per cent.^{3,15} Spector *et al.* showed equivalent results with radiotherapy and conservation surgery for T_2 glottic lesions.²⁵

In our series, four patients (18 per cent) with T_3 laryngeal lesions who were given primary radiotherapy developed a local recurrence. This is a small series and there may be selection bias, as 45 per cent of patients with T_3 lesions were treated with primary surgery. In the literature, local control rates after radiotherapy for T_3 glottic lesions range from 57 to 65 per cent.^{15,16,21} In the series published by Johansen *et al.*, the five-year local rate for T_3 glottic tumours was 48 per cent and for T_4 tumours was 38 per cent.²⁴ Another study of 116 patients achieved similar results with surgery and post-operative radiotherapy.²⁶ Local control rates after radiotherapy for T_4 glottic lesions range from 50 to 60 per cent.^{15,22}

The five-year survival rate for the entire group of patients in our series (n = 202) was 69 per cent. The five-year crude survival in North America was about 67 per cent for glottic tumours and 41 per cent for supraglottic tumours²⁷ and the rate for glottic tumours in a series from Denmark was 66 per cent.²⁴

Multivariate analysis by Mendenhall *et al.* of their data for treatment of T_1 and T_2 glottic lesions by radiotherapy showed that histological differentiation significantly influenced local control and cause-specific survival.²⁸ Other parameters reported to affect cure included pretreatment haemoglobin⁶ and Karnofsky performance.²⁹ In our series, age and T stage significantly affected overall survival.

The best measure of the efficacy of a treatment modality for cure of the primary tumour is evaluation of local control after treatment.²⁰ The importance of achieving primary locoregional control for disease-specific survival was highlighted by Johansen *et al.*, who demonstrated that 93 per cent of their patients with supraglottic carcinomas treated with radiotherapy who achieved locoregional control survived 10 years, whereas only 29 per cent of patients who failed locally or regionally survived 10 years.¹⁴

Our strategy has always been to treat carcinoma of the larynx with the aim of preserving the laryngeal voice and of reserving surgery for salvage or advanced-stage tumours. Our current treatment protocol for patients with laryngeal carcinoma includes standard radiotherapy, accelerated radiotherapy, chemoradiotherapy and surgery. Patients with T_1 and non-bulky T_2 N₀ carcinomas of the larynx are treated with standard radiotherapy of 66–70 Gy. Patients with bulky $T_2 N_0$ carcinomas of the larynx, or stage III or IV disease without distant metastases, are treated with accelerated radiotherapy using a concomitant boost. Alternatively, patients with stage III or IV disease who have acceptable renal function may be offered either neo-adjuvant, concurrent or adjuvant chemotherapy.

One study by the Radiation Therapy Oncology Group showed that accelerated radiotherapy with a concomitant boost or hyperfractionated radiotherapy was better than standard fractionation for locoregional control.³⁰ Recent data suggest that concurrent chemoradiotherapy is superior to radiotherapy alone for advanced-stage laryngeal disease.³¹ Similarly, concurrent chemotherapy is superior to induction chemotherapy followed by radiotherapy or radiotherapy alone for laryngeal preservation and locoregional control in patients with laryngeal carcinoma.³²

Patients with T_3 and non-bulky T_4 lesions of the larynx or those with smaller lesions but positive neck nodes are now treated with concurrent chemoradiotherapy, surgery and post-operative radiotherapy, or primary accelerated radiotherapy. The choice will depend on various factors, such as the patient's ability to receive chemotherapy and their willingness to undergo surgery. Patients with bulky T₄ carcinomas are treated with a total laryngectomy and post-operative radiotherapy or concurrent chemoradiotherapy. Patients requiring a pretreatment tracheostomy due to their disease are treated with concurrent chemoradiotherapy or with a total laryngectomy and post-operative radiotherapy. Patients with extensive T₄ lesions are offered a total laryngectomy. For patients who undergo primary surgery for advanced head and neck carcinomas, two recent studies have shown that post-operative concurrent radiotherapy chemotherapy with significantly improves local and regional control and diseasefree survival when compared with post-operative radiotherapy alone.33,34

Conclusions

We have analysed and presented the five-year survival rates and patterns of failure of a series of 202 patients with laryngeal carcinoma treated with either radiotherapy, or surgery and post-operative radiotherapy, at the Prince of Wales Hospital, Hong Kong, between 1990 and 1999. The median follow-up period of patients who were alive at the time of the study was 60 months. Eighteen patients (9 per cent) had persistent disease, and 24 patients (17 per cent) had local recurrence at the primary site after treatment. The five-year overall local control rate was 86 per cent and the ultimate local control rate was 93 per cent. Ten patients (5 per cent) developed regional recurrence and none of the factors analysed significantly influenced regional failure. The five-year regional control rate was 96 per cent. The five-year relapse-free survival rate was 82 per cent, and none of the factors analysed significantly affected relapse-free survival. The five-year overall survival rate was 69 per cent, with age and T stage significantly affecting overall survival. Our results are in keeping with results published by other institutions for similar disease and treatment strategies.

- This study is a retrospective analysis of the five-year survival rates and patterns of failure of 202 Hong Kong patients with laryngeal carcinoma treated with either radiotherapy or surgery and post-operative radiotherapy with the intention to cure during the 10-year study period
- The overall five-year survival rate for laryngeal carcinoma treated with primary or post-operative radiotherapy was 69 per cent
- Radiotherapy for early glottic carcinoma preserves the voice quality when compared with other forms of treatment and has similar cure rates
- Treatment options for laryngeal carcinoma are discussed

References

- 1 The Department of Veteran Affairs Laryngeal Cancer Study Group. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. *N Engl J Med* 1991;**324**:1685–90
- 2 American Joint Committee on Cancer. *AJCC Cancer Staging Manual*, 5th edn. Philadelphia: Lippincott-Raven, 1997
- 3 Lee DJ. Definitive radiotherapy for squamous carcinoma of the larynx. *Otolaryngol Clin N Am* 2002;**35**:1013–33
- 4 Jorgensen K, Godballe C, Hansen O, Bastholt L. Cancer of the larynx. Treatment results after primary radiotherapy with salvage surgery in a series of 1005 patients. Acta Oncol 2002;41:69-72
- 5 van der Voet JC, Keus RB, Hart AA, Hilgers FJ, Bartelink H. The impact of treatment time and smoking on local control and complications in T1 glottic cancer. *Int J Radiat Oncol* 1998;**42**:247–55
- 6 Warde P, O'Sullivan B, Bristow RG, Panzarella T, Keane TJ, Gullane PJ *et al.* T1/T2 glottic cancer managed by external beam radiotherapy: the influence of pretreatment hemoglobin on local control. *Int J Radiat Oncol* 1998;**41**: 347–53
- 7 Steiner W. Results of curative laser microsurgery of laryngeal carcinomas. *Am J Otolaryngol* 1993;**14**:116–21
- 8 Moreau PR. Treatment of laryngeal carcinomas by laser endoscopic microsurgery. Laryngoscope 2000;110:1000-6
- 9 Rydell R, Schalen L, Fex S, Elner A. Voice evaluation before and after laser excision vs. radiotherapy of T1A glottic carcinoma. Acta Oto Laryngol 1995;115:560–5
- glottic carcinoma. Acta Oto Laryngol 1995;115:560-5
 10 Blakeslee D, Vaughn CW, Shapshay SM, Simpson GT, Strong MS. Excisional biopsy in the selective management of T1 glottic cancer: a three-year follow-up study. Laryngoscope 1984;94:488-94
- 11 Ossoff RH, Sission GA, Shapshay SM. Endoscopic management of selected early vocal carcinoma. *Ann Otol Rhinol Laryngol* 1985;94:560–4
- 12 DiNardo LJ, Kaylie DM, Isaacson J. Current treatment practices for early laryngeal carcinoma. *Otolaryngol Head Neck Surg* 1999;**120**:30–7
- 13 Chevalier D, Laccourreye O, Brasnu D, Laccourreye H, Piquet JJ. Cricohyoidoepiglottopexy for glottic carcinoma with fixation or impaired motion of the true vocal cord: 5-year oncologic results with 112 patients. Ann Otol Rhinol Laryngol 1997;106:364–9
- Rhinol Laryngol 1997;106:364–9
 14 Johansen LV, Grau C, Overgaard J. Suparglottic carcinoma: patterns of failure and salvage treatment after curatively intended radiotherapy in 410 consecutive patients. *Int J Radiat Oncol* 2002;53:948–58
- 15 Harwood AR. Cancer of the larynx. The Toronto experience. J Otolaryngol 1982;11:3-21

- 16 Wang CC. Carcinoma of the larynx. In: Wang CC, ed. Radiation Therapy For Head And Neck Neoplasms: Indications, Techniques and Results. Chicago: Year Book Medical Publishers, 1997;221–55
- 17 Bataini JP, Ennuyer A, Poncet P, Ghossein NA. Treatment of supraglottic cancer by radical high dose radiotherapy. *Cancer* 1974;**33**:1253–62
- 18 Wall TJ, Peters LJ, Brown BW, Oswald MJ, Milas L. Relationship between lymph node status and primary tumor control probability in tumors of the supraglottic larynx. *Int J Radiat Oncol* 1985;**11**:1895–02
- 19 Mendenhall WM, Parsons JT, Mancuso AA, Stringer SP, Cassisi NJ. Radiotherapy for squamous cell carcinoma of the supraglottic larynx: an alternative to surgery. *Head Neck* 1996;18:24–35
- 20 Hinerman RW, Mendenhall WM, Amdur RJ, Stringer SP, Villaret DB, Robbins KT. Carcinoma of the supraglottic larynx: treatment results with radiotherapy alone or with planned neck dissection. *Head Neck* 2002;24:456–67
- 21 Mendenhall WM. T3–4 squamous cell carcinoma of the larynx treated with radiation therapy alone. *Semin Radiat Oncol* 1998;8:262–9
- 22 Paisley S, Warde PR, O'Sullivan B, Waldron J, Gullane PJ, Payne D *et al*. Results of radiotherapy for primary subglottic squamous cell carcinoma. *Int J Radiat Oncol* 2002;**52**: 1245–50
- 23 Eckel HE. Local recurrences following transoral laser surgery for early glottic carcinoma: frequency, management, and outcome. Ann Oto Rhino Laryngol 2001;110: 7–15
- 24 Johansen LV, Grau C, Overgaard J. Glottic carcinoma patterns of failure and salvage treatment after curative radiotherapy in 861 consecutive patients. *Radiother Oncol* 2002;63:257–67
- 25 Spector JG, Sessions DG, Chao KS, Hanson JM, Simpson JR, Perez CA. Management of stage II (T2N0M0) glottic carcinoma by radiotherapy and conservation surgery. *Head Neck* 1999;**21**:116–23
- 26 Nguyen TD, Malissard L, Theobald S, Eschwege F, Panis X, Bachaud JM *et al.* Advanced carcinoma of the larynx: results of surgery and radiotherapy without induction chemotherapy (1980–1985): a multivariate analysis. *Int J Radiat Oncol* 1996;**36**:1013–18
- 27 Skarsgard DP, Groome PA, MacKillop WJ, Zhou S, Rothwell D, Dixon PF *et al.* Cancers of the upper aerodigestive tract in Ontario, Canada, and the United States. *Cancer* 2000;88:1728–38
- 28 Mendenhall WM, Amdur RJ, Morris CG, Hinerman RW. T1–T2 N0 squamous cell carcinoma of the glottic larynx treated with radiation therapy. *J Clin Oncol* 2001;19: 4029–36

- 29 Narayana A, Vaughan AT, Kathuria S, Fisher SG, Walter SA, Reddy SP. P53 overexpression is associated with bulky tumor and poor local control in T1 glottic cancer. *Int J Radiat Oncol* 2000;**46**:21–6
- 30 Fu KK, Pajak TF, Trotti A, Jones CU, Spencer SA, Phillips TL et al. A Radiation Therapy Oncology Group (RTOG) phase III randomized study to compare hyperfractionation and two variants of accelerated fractionation to standard fractionation radiotherapy for head and neck squamous cell carcinomas: first report of RTOG 9003. Int J Radiat Oncol 2000;48:7–16
- 31 Pignon JP, Bourhis J, Domenge C, Designe L. Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: three meta-analyses of updated individual data. MACH-NC Collaborative Group. Meta-Analysis of Chemotherapy on Head and Neck Cancer. *Lancet* 2000;355:949–55
- 32 Forastiere AA, Goepfert H, Maor M, Pajak TF, Weber R, Morrison W *et al.* Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med* 2003;**349**:2091–8
- 33 Cooper JS, Pajak TF, Forastiere AA, Jacobs J, Campbell BH, Saxman SB *et al.* Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. *N Engl J Med* 2004;**350**: 1937–44
- 34 Bernier J, Domenge C, Ozsahin M, Matuszewska K, Lefebvre JL, Greiner RH *et al.* Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *N Engl J Med* 2004;**350**: 1945–52

Address for correspondence: Professor C Andrew van Hasselt, Chairman and Professor, Department of Surgery, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin NT, Hong Kong SAR, China.

Fax: +(852) 2646 6312 E-mail: andrewvan@cuhk.edu.hk

Dr A C Vlantis takes responsibility for the integrity of the content of the manuscript. Competing interests: None declared